

Response - March 6, 2007  
U.S. Application Serial No. 10/775,647

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REMARKS

Minor amendments are made to claims 5-9 and 11-15 to change dependencies.

Rejection of Claims 4-15 Under 35 U.S.C. § 103(a)-

The Examiner has rejected claims 4-15 under 35 U.S.C. § 103(a) as being obvious over WO 96/24661 and/or U.S. Patent No. 5,695,998 (the '998 patent) taken with Gottrup et al., U.S. Patent No. 5,759,830 (the '830 patent), and U.S. Patent No. 4,829,000 (the '000 patent). Applicants respectfully traverse the Examiner's rejection. Claims 4-15 are not obvious over WO 96/24661 and/or the '998 patent taken with Gottrup et al., the '830 patent, and the '000 patent.

MPEP § 2143 titled "Basic Requirements of a *Prima Facie* Case of Obviousness" reads as follows:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

MPEP § 2143. Thus, MPEP § 2143 and the case law that it cites require that there must be some suggestion or motivation to modify the reference or to combine reference teachings with a reasonable expectation of success in reaching the claimed invention.

All of the rejected claims 4-15 require the step of contacting "cells *in vitro* with a *cell growth substrate comprising stomach submucosal tissue*." None of the cited references, alone or in combination, mentions or suggests using stomach submucosal tissue as a cell growth substrate. In fact, the word stomach does not appear in any of the cited references (WO

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96/24661, the '998 patent, the '830 patent, or the '000 patent) except Gottrup et al. The only description of stomach tissue in Gottrup et al. is a disclosure that stomach tissue comprises collagen. As stated by the Examiner, WO 96/24661 and the '998 patent teach the use of *intestinal submucosa* for culturing cells (See page 3 of the September 6, 2006 office action). The '830 patent teaches the use of collagen to promote attachment of cells to matrices comprising synthetic polymers, and the '000 patent teaches the use of a complex basement membrane extract for culturing cells. Thus, none of the cited references, alone or in combination, mentions or suggests using stomach submucosal tissue as a cell growth substrate.

The Examiner contends that because WO 96/24661, the '998 patent, the '000 patent, and the '830 patent describe either 1.) a collagen-containing extracellular matrix material for use in growing cells (WO 96/24661, the '998 patent, and the '000 patent) or 2.) a matrix made of a synthetic polymer coated with collagen for use in growing cells (the '830 patent), the cited references suggest the use of a collagen-containing matrix material as a cell growth substrate. The Examiner further contends that stomach tissue comprises collagen (Gottrup et al.) so a skilled artisan would have been motivated to substitute the intestinal submucosa-containing collagenous matrices described in WO 96/24661 and the '998 patent with stomach submucosal tissue for use as a growth substrate, as claimed in Applicants' claims 4-15, because collagen-containing matrices are known for use as cell growth substrates and stomach tissue contains collagen. The Examiner states that "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute stomach submucosa for intestinal submucosa in the method for culturing eukaryotic cells" because "both stomach submucosa and intestinal submucosa contain collagen" (See bottom of page 3 to top of page 4 of the September 6, 2006 office action).

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Thus, the Examiner is arguing that the cited reference combination suggests a method comprising the step of contacting "cells *in vitro* with a cell growth substrate comprising stomach submucosal tissue" because the collagen-containing matrices described in the cited references promote cell growth and stomach tissue contains collagen. The flaw in the Examiner's argument is that none of the references, alone or in combination, describes a matrix that contains only collagen (*i.e.*, all of the references describe complex matrices comprising multiple components) and none of the references, alone or in combination, indicate that collagen is the factor in the matrix composition that promotes cell growth. Accordingly, it would not have been obvious to substitute stomach submucosal tissue for the intestinal submucosa tissue compositions described in WO 96/24661 and the '998 patent simply because stomach tissue comprises collagen. Moreover, the '830 patent discourages such a modification.

For example, WO 96/24661 and the '998 patent describe collagenous matrices that comprise a variety of different components including collagens, glycoproteins, proteoglycans, glycosaminoglycans, and other factors. No where does WO 96/24661 or the '998 patent conclude that collagen is the factor that promotes cell growth in these complex compositions. The '000 patent describes a complex basement membrane extract composition that comprises laminin, type IV collagen, heparin sulfate, proteoglycans, entactin, nidogen, and other components. No where does the '000 patent conclude that collagen is the factor that promotes cell growth in the complex compositions described in the '000 patent.

Lastly, the '830 patent describes synthetic polymers for use as cell growth substrates in combination with many other factors where collagen is described as being a factor for *cell attachment, not cell growth*. As stated in the '830 patent, the *attachment* of the cells to the polymer is enhanced by coating the polymers with compounds such as basement membrane components, agar, agarose, gelatin, gum arabic, *collagens types I, II, III, IV, and V*, fibronectin,

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laminin, glycosaminoglycans, mixtures thereof, and other materials known to those skilled in the art of cell culture. No where does the '830 patent conclude that collagen is the factor that promotes cell growth in the compositions described in the '830 patent. In fact, Fig. 22 a.-c. in the '830 patent describe assays where cells are overlayed with collagen layers of varying thicknesses. The cells in the control wells double in number in twenty-four hours. In contrast, cells overlayed with collagen layers show markedly diminished cell number, or, in some cases, all of the cells overlayed with collagen have rounded and have died (see also Fig. 21b in the '830 patent). Thus, none of the cited references, alone or in combination, suggests that collagen is a cell growth-promoting factor. In fact, the '830 patent suggests that collagen is NOT a growth-promoting factor.

Thus, the Examiner's argument is flawed. It would not have been obvious at the time the invention was made to substitute the intestinal submucosa compositions described in WO 96/24661 and the '998 patent with stomach submucosal tissue because stomach tissue contains collagen. The reference combination provides no suggestion that stomach tissue would function effectively as a cell growth substrate, and should be substituted for the intestinal submucosa compositions described in WO 96/24661 and the '998 patent because stomach tissue contains collagen. In fact, the '830 patent suggests the opposite. Therefore, the cited references do not render the invention of claims 4-15 obvious because the reference combination does not suggest modifying the intestinal submucosa compositions described in WO 96/24661 and the '998 patent with stomach submucosal tissue to reach the claimed invention. Withdrawal of the rejection of claims 4-15 under 35 U.S.C. § 103(a) is respectfully requested.

**Rejection of Claims 4-15 for Obviousness-Type Double Patenting-**

The Examiner has also rejected claims 4-15 for obviousness-type double patenting

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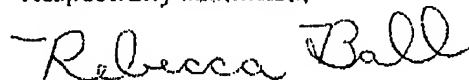
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over claim 1 of the '998 patent based on the same reasoning as discussed above. Therefore, the arguments discussed in the preceding section apply with equal force to this rejection, but in the context of obviousness-type double patenting. Moreover, claims 4-15 in the instant application are not obvious over claim 1 of the '998 patent because a new submucosa tissue (*i.e.*, stomach submucosa tissue) is specified in the claims of the instant application. Also, the subject matter of the dependent claims 5-9 and 11-15 is not obvious over claim 1 of the '998 patent, and the Examiner has provided no arguments relative to obviousness of the dependent claims over claim 1 of the '998 patent. Withdrawal of the rejection of claims 4-15 for obviousness-type double patenting is respectfully requested.

#### CONCLUSION

The foregoing remarks are believed to fully respond to the Examiner's rejections. The claims are in condition for allowance. Applicants respectfully request allowance of the claims, and passage of the application to issuance.

Respectfully submitted,



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